

doxycycline per day or placebo. Patients will be seen monthly during the medication phase and at 18 months. Physical function will be evaluated before treatment starts, and at 3, 6, 9, 12 and 18 months. Patients will also complete questionnaires designed to provide measures of pain, fatigue, and neurocognitive dysfunction.

Another project, funded by the DoD and conducted by the Louisiana Medical Foundation, involves blinded and placebo-controlled clinical trials of antibiotic treatment of patients who are experiencing chronic non-specific symptoms and who show bacterial remnants in their urine (DoD research project # 67; RWG, 1998; 1999). This trial is expected to be completed in 1999.

6. Concluding Remarks

During the upcoming two-and-a-half day conference, participants from various disciplines will meet several times in workgroups with the goal of discussing and recommending research in one of four focus areas related to illnesses among Gulf War veterans:

- C Workgroup 1: Pathophysiology, Etiology, and Mechanisms of Action;
- C Workgroup 2: Assessment/Diagnosis;
- C Workgroup 3: Treatment; and
- C Workgroup 4: Prevention.

A central question to be addressed by Workgroup 1 is: What are the most plausible etiological hypotheses concerning 1) diagnosed diseases and 2) unexplained multiple-symptom illnesses noted among Gulf War veterans? Associated questions include: Are ongoing research projects addressing the most plausible of these hypotheses? If not, which additional plausible hypotheses should be addressed? Are there research methods or approaches that need to be developed, or that are available and not being used? The Gulf War experience has created interest in the health effects of particular chemical agents, such as depleted uranium, organophosphate chemical warfare nerve agents, carbamate prophylactic agents against organophosphate nerve agents, vaccines, and organophosphate pesticides. This interest leads to additional questions within the focus of Workgroup 1. Should additional research resources be applied to better understand exposure-response relationships for, mechanisms of actions of, individual susceptibility to, and/or biomarkers of exposure to specific chemical agents or classes of agents associated with the Gulf War experience? Are current research efforts to examine potential interactions among “Gulf war mixtures” of chemicals and other health risk factors of sufficient scope and design? What alternative research approaches could be taken to decrease the uncertainty that will exist in any future attempts to extrapolate results from the animal “mixtures” experiments to expected human exposure scenarios? Should such research efforts be made?

Results from several epidemiological studies concur that Gulf War veterans more frequently report multiple symptoms of ill health than non-deployed veterans of the same era and that there may be an increased frequency of chronic, multi-systemic conditions of ill health among groups of Gulf War veterans. The array of reported symptoms are, in general, difficult to diagnose into a disease category. The most frequently reported chronic symptoms among Gulf War veterans with

unexplained or undiagnosed illnesses in the DoD and DVA clinical programs (fatigue, headache, memory problems, sleep disturbances, skin rash, joint pain, and shortness of breath) and in epidemiology studies appear to overlap with several of the symptoms in other symptom-based disorders including chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity. Using factor analysis to examine associations among self-reported symptoms in different sets of Gulf War veterans, one group of investigators proposed that there might be unique disorders among Gulf War veterans (Haley et al., 1997a,b; Haley and Kurt, 1997), whereas other groups concluded that evidence for a unique Gulf War syndrome was not found when control groups were included in the analysis (Fukuda et al., 1998; Ismail et al., 1999). These results are within the focus of Workgroup 2 and lead to several questions related to the goal of recommending research on the assessment and diagnosis of illnesses among Gulf War veterans. Are ongoing efforts to assess the prevalence of these and other illnesses among Gulf war veterans of sufficient scope and design? What are the best or optimal research approaches and methods to apply to the question of whether or not there are unique health conditions among Gulf War veterans? (i.e., are there Gulf War syndromes?) Are ongoing projects using these approaches and methods to address the issues of assessing and diagnosing illnesses among Gulf War veterans? Are there particular clinical and/or research methods or approaches that need further development or validation before they can be used to assess or diagnose illnesses among Gulf War veterans? Which of these methods or approaches hold the greatest promise in increasing the efficiency and accuracy of assessing and diagnosing illnesses among Gulf War veterans or veterans of future wars?

In response to the wide diversity of illnesses and symptoms experienced by Gulf War veterans and the uncertainty of their cause, several reviewers (Engel et al., 1998; Joseph et al., 1998; Lashof and Cassells, 1998) have noted that treatment should proceed on an individual basis and is best addressed when objective clinical measures of distinct illness can be made and that, in the absence of such measures, multidisciplinary treatment of symptoms may be effective. Questions of relevance to the focus of Workgroup 3 include: What are likely to be the most appropriate treatment and/or rehabilitation approaches for 1) veterans with the most frequently diagnosed categories of diseases and 2) veterans with unexplained multiple-symptom illnesses? Are ongoing clinical trials of treatment options (e.g., antibiotic treatment trials and multidisciplinary treatment trials) of appropriate scope, size, and design? Are there other potentially useful treatment approaches or methods that need more basic research before development? Is there a need to educate physicians concerning options in treating Gulf War veterans with illnesses? Are there sufficient health care opportunities for Gulf War veterans?

Joseph et al. (1988) have noted that the DoD has recognized recommendations from various scientific review panels and government agency groups of the need for improved health surveillance programs for military personnel before, during, and after deployment to combat situations, in order to decrease uncertainties regarding chronic, post-deployment health consequences. Components of the surveillance programs include enhancing capabilities of identifying individuals with health risks, conducting standardized health assessments before and after deployment, assessing and documenting exposures to hazardous substances through

environmental monitoring and/or biomonitoring, and monitoring health status of personnel after deployment (Joseph et al., 1988). Questions related to the focus of Workgroup 4, Prevention, include: How can health surveillance programs for U.S. military personnel be improved to decrease uncertainties about post-deployment health consequences? What types of health risk communication and education programs will be useful to prevent or minimize exposure to the most likely chemical and biological health hazards in future conflicts? What techniques or methods of environmental monitoring or biomonitoring are likely to be most useful in helping to prevent or minimize exposure to chemical or biological agents in future conflicts? Which of these require further research and development? What prophylactic methods are available against the most likely chemical and biological health hazards to be encountered in future conflicts? Which of these require further research and development?

Workgroups will meet for discussion and deliberation during four sessions of 2- to 3-hour duration. Final reports and recommendations from each Workgroup will be presented to the conference at large prior to adjournment.

7. References

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